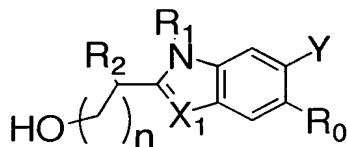


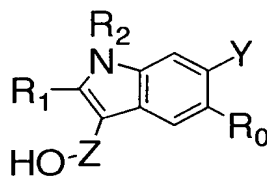
## WHAT IS CLAIMED IS

1. A compound having the formula



(I)

or



(II)

in which:

$R_0$  is selected from the group consisting of  $C_1$ - $C_3$  alkyl, cyclopropyl, halo,  $OR_5$  and  $S(O)_mR_5$  in which  $m$  is 0, 1 or 2;

$R_1$  and  $R_2$  are independently selected from the group consisting of  $C_2$ - $C_8$  alkenyl, phenylcyclopropyl, phenylpropenyl,  $R_6-X_2-C(R_8)(R_8)-R_7$ ; and  $R_6-X_2-N(R_8)-R_7$ ;

$R_3$  and  $R_4$  are independently hydrogen, methyl or ethyl;

$R_5$  is methyl or ethyl;

$R_6$  is selected from the group consisting of hydrogen,  $C_1$ - $C_{10}$  alkyl, aryl, W, Y,  $NH_2$ ,  $NHCONR_3R_4$ ,  $NHCOOR_3$  and  $NHSO_2R_9$ ;

$R_7$  is selected from the group consisting of a direct bond, an alkyl group having from 1 to 10 carbon atoms, aryl,  $-(NH)_p(CH_2CH_2O)_q(NH)_p-$  in which  $p$  is 0 or 1 and  $q$  is an integer from 1 to 4, and W;

R<sub>8</sub> is selected from the group consisting of H, Y, OH, -NHCONR<sub>3</sub>R<sub>4</sub>; -NHCOOR<sub>3</sub>; -NHSO<sub>2</sub>R<sub>9</sub>, -(CH<sub>2</sub>)<sub>r</sub>CO<sub>2</sub>R<sub>3</sub>, and (CH<sub>2</sub>)<sub>r</sub>CO<sub>2</sub>NR<sub>3</sub>R<sub>4</sub> in which *r* is an integer from 1 to 3;

R<sub>9</sub> is aryl or C<sub>1</sub>-C<sub>6</sub> alkyl;

5 X<sub>1</sub> is -CH-, -C-hal, -C(CH<sub>3</sub>) or -C(C<sub>2</sub>H<sub>5</sub>), in which *hal* stands for a halogen atom (preferably chloro, fluoro or bromo);

X<sub>2</sub> is selected from the group consisting of a direct bond, -NH-, -N(CH<sub>3</sub>)-, -NCONR<sub>3</sub>R<sub>4</sub>-, -NCOOR<sub>3</sub>-, and NSO<sub>2</sub>R<sub>9</sub>;

W is a saturated carbocyclic or heterocyclic group;

10 Y is selected from the group consisting of COOH, COOR<sub>3</sub>, CONR<sub>3</sub>R<sub>4</sub>, CONHSO<sub>2</sub>R<sub>5</sub>, hydroxymethyl, -CH<sub>2</sub>COOH, CH<sub>2</sub>CONR<sub>3</sub>R<sub>4</sub>; and 5-tetrazolyl; and

Z is -CH<sub>2</sub>-, -CH(CH<sub>3</sub>)-, C(CH<sub>3</sub>)<sub>2</sub>- or -CO-;

and hydrates and salts thereof, and labeled derivatives thereof.

2. A compound of Formula (I) according to claim 1.

3. A compound of Formula (II) according to claim 1.

15 4. A compound according to claim 1 in which Y is COOH or COOR<sub>3</sub>.

5. A compound according to claims 1 in which R<sub>0</sub> is a C<sub>1</sub>-C<sub>3</sub> alkyl group.

6. A compound according to claim 5 in which R<sub>0</sub> is methyl.

7. A compound according to claim 2 in which R<sub>1</sub> is optionally substituted phenethyl.

20 8. A compound according to claim 2 in which R<sub>1</sub> is 2-hydroxyethyl.

9. A compound according to claim 2 in which R<sub>2</sub> is n-butyl, phenyl or n-butyrylamido.

10. A compound according to claim 2 in which R<sub>2</sub> is R<sub>6</sub>-X<sub>2</sub>-C(R<sub>8</sub>)(R<sub>8</sub>)-R<sub>7</sub>- or R<sub>6</sub>-X<sub>2</sub>-N(R<sub>8</sub>)-R<sub>7</sub>-, and the group R<sub>6</sub>-X<sub>2</sub>-C(R<sub>8</sub>)(R<sub>8</sub>)-R<sub>7</sub>- or R<sub>6</sub>-X<sub>2</sub>-N(R<sub>8</sub>)-R<sub>7</sub>- is selected from  
25 C<sub>3</sub>-C<sub>8</sub> alkyl; C<sub>3</sub>-C<sub>6</sub> cycloalkyl; C<sub>3</sub>-C<sub>8</sub> alkenyl; -(CH<sub>2</sub>)<sub>m</sub>C<sub>6</sub>H<sub>5</sub> where *m* is 0 or an integer from

1-3;  $-\text{CH}_2\text{OC}_6\text{H}_5$ ,  $\text{CH}_2\text{COC}_6\text{H}_5$ , phenyl( $\text{C}_2\text{-C}_4$  alkenyl), or analogous moieties having substituted phenyl groups; optionally substituted phenylcyclopropyl;  $-(\text{CH}_2)_s\text{OH}$ ,  $-(\text{CH}_2)_s\text{CONH}_2$  and  $-(\text{CH}_2)_s\text{COOH}$  where  $s$  is an integer from 1 to 3; phenyl; thienyl; and optionally substituted  $\text{C}_3\text{-C}_6$  cycloalkyl-( $\text{C}_1\text{-C}_3$  alkyl).

- 5                    11.     A compound according to claim 2 in which  $\text{R}_0$  is methyl,  $\text{R}_1$  is phenethyl,  $\text{R}_2$  is n-butyl,  $\text{X}_1$  is  $-\text{CH}$ ,  $\text{Y}$  is  $\text{COOH}$  and  $n$  is 0.
12.     A compound according to claim 2 in which  $\text{R}_0$  is methyl,  $\text{R}_1$  is 2-hydroxyethyl,  $\text{R}_2$  is n-butyl,  $\text{X}_1$  is  $-\text{CH}$ ,  $\text{Y}$  is  $\text{COOH}$  and  $n$  is 0.
13.     A compound according to claim 3 in which  $\text{R}_2$  is phenethyl or 2-  
10    hydroxyethyl.
14.     A compound according to claim 3 in which  $\text{R}_1$  is  $\text{C}_3\text{-C}_8$  alkyl.
15.     A compound according to claim 3 in which  $\text{R}_0$  is methyl,  $\text{R}_1$  is n-pentyl,  $\text{R}_2$  is phenethyl,  $\text{X}_1$  is  $-\text{CH}$  and  $\text{Y}$  is  $\text{COOH}$ .
16.     A probe comprising a compound according to claim 1 and a detectable  
15    label.
17.     A method for inhibiting the functioning of a PDZ domain of a protein comprising contacting the protein with an inhibitory effective amount of a compound according to claim 1.
18.     A method for inhibiting the functioning of a PDZ domain of a protein  
20    comprising contacting the protein with an inhibitory effective amount of a compound according to claim 2.
19.     A method for inhibiting the functioning of a PDZ domain of a protein comprising contacting the protein with an inhibitory effective amount of a compound according to claim 3.
- 25                    20.     A method for inhibiting the functioning of a PDZ domain of a protein comprising contacting the protein with an inhibitory effective amount of a compound according to claim 7.

21. A method for inhibiting the functioning of a PDZ domain of a protein comprising contacting the protein with an inhibitory effective amount of a compound according to claim 8.

22. A method for inhibiting the functioning of a PDZ domain of a protein comprising contacting the protein with an inhibitory effective amount of a compound according to claim 9.

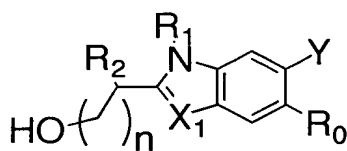
23. A method for inhibiting the functioning of a PDZ domain of a protein comprising contacting the protein with an inhibitory effective amount of a compound according to claim 10.

24. A method for inhibiting the functioning of a PDZ domain of a protein comprising contacting the protein with an inhibitory effective amount of a compound according to claim 11.

25. A method for inhibiting the functioning of a PDZ domain of a protein comprising contacting the protein with an inhibitory effective amount of a compound according to claim 15.

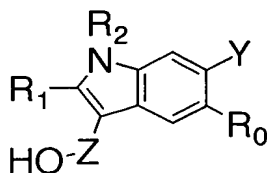
26. A method according to claim 17 in which the protein is a MAGI protein.

27. A combinatorial library of two or more compounds having the formula



(I)

or



(II)

in which:

R<sub>0</sub> is selected from the group consisting of C<sub>1</sub>-C<sub>3</sub> alkyl, cyclopropyl, halo, OR<sub>5</sub> and S(O)<sub>m</sub>R<sub>5</sub> in which *m* is 0, 1 or 2;

- 5 R<sub>1</sub> and R<sub>2</sub> are independently selected from the group consisting of C<sub>2</sub>-C<sub>8</sub> alkenyl, phenylcyclopropyl, phenylpropenyl, R<sub>6</sub>-X<sub>2</sub>-C(R<sub>8</sub>)(R<sub>8</sub>)-R<sub>7</sub>-; and R<sub>6</sub>-X<sub>2</sub>-N(R<sub>8</sub>)-R<sub>7</sub>-;

R<sub>3</sub> and R<sub>4</sub> are independently hydrogen, methyl or ethyl;

R<sub>5</sub> is methyl or ethyl;

- 10 R<sub>6</sub> is selected from the group consisting of hydrogen, C<sub>1</sub>-C<sub>10</sub> alkyl, aryl, W, Y, NH<sub>2</sub>, NHCONR<sub>3</sub>R<sub>4</sub>, NHCOOR<sub>3</sub> and NHSO<sub>2</sub>R<sub>9</sub>;

R<sub>7</sub> is selected from the group consisting of a direct bond, an alkyl group having from 1 to 10 carbon atoms, aryl, -(NH)<sub>p</sub>(CH<sub>2</sub>CH<sub>2</sub>O)<sub>q</sub>(NH)<sub>p</sub>- in which *p* is 0 or 1 and *q* is an integer from 1 to 4, and W;

- 15 R<sub>8</sub> is selected from the group consisting of H, Y, OH, -NHCONR<sub>3</sub>R<sub>4</sub>; -NHCOOR<sub>3</sub>; -NHSO<sub>2</sub>R<sub>9</sub>, -(CH<sub>2</sub>)<sub>r</sub>CO<sub>2</sub>R<sub>3</sub>, and (CH<sub>2</sub>)<sub>r</sub>CO<sub>2</sub>NR<sub>3</sub>R<sub>4</sub> in which *r* is an integer from 1 to 3;

R<sub>9</sub> is aryl or C<sub>1</sub>-C<sub>6</sub> alkyl;

X<sub>1</sub> is -CH-, -C-hal, -C(CH<sub>3</sub>) or -C(C<sub>2</sub>H<sub>5</sub>), in which *hal* stands for a halogen atom (preferably chloro, fluoro or bromo);

- 20 X<sub>2</sub> is selected from the group consisting of a direct bond, -NH-, -N(CH<sub>3</sub>)-, -NCONR<sub>3</sub>R<sub>4</sub>-, -NCOOR<sub>3</sub>-, and NSO<sub>2</sub>R<sub>9</sub>;

W is a saturated carbocyclic or heterocyclic group;

Y is selected from the group consisting of COOH, COOR<sub>3</sub>, CONR<sub>3</sub>R<sub>4</sub>, CONHSO<sub>2</sub>R<sub>5</sub>, hydroxymethyl, -CH<sub>2</sub>COOH, CH<sub>2</sub>CONR<sub>3</sub>R<sub>4</sub>; and 5-tetrazolyl; and

Z is -CH<sub>2</sub>-, -CH(CH<sub>3</sub>)-, C(CH<sub>3</sub>)<sub>2</sub>- or -CO-;

- 25 and hydrates and salts thereof, and labeled derivatives thereof.

28. A combinatorial library according to claim 27 in which the compounds are of Formula (I).

29. A combinatorial library according to claim 27 in which the compounds are of Formula (II).

30. A method for screening one or more proteins for PDZ domain activity comprising contacting the one or more proteins with a compound according to claim 1.

5 31. An array for screening for PDZ domain activity or inhibition of the same, or for studying protein-protein interactions comprising two or more compounds according to claim 1.

10 32. A method for treating a cancer in cancerous cells or in a patient comprising contacting the cancerous cells with, or administering to the patient, a therapeutically effective amount of a compound according to claim 1.

33. A method for treating a cancer in a patient comprising administering to the patient a therapeutically effective amount of a compound according to claim 2.

34. A method for treating a cancer in a patient comprising administering to the patient a therapeutically effective amount of a compound according to claim 3.

15 35. A method for treating a cancer in a patient comprising administering to the patient a therapeutically effective amount of a compound according to claim 11.

36. A method for treating a cancer in a patient comprising administering to the patient a therapeutically effective amount of a compound according to claim 15.